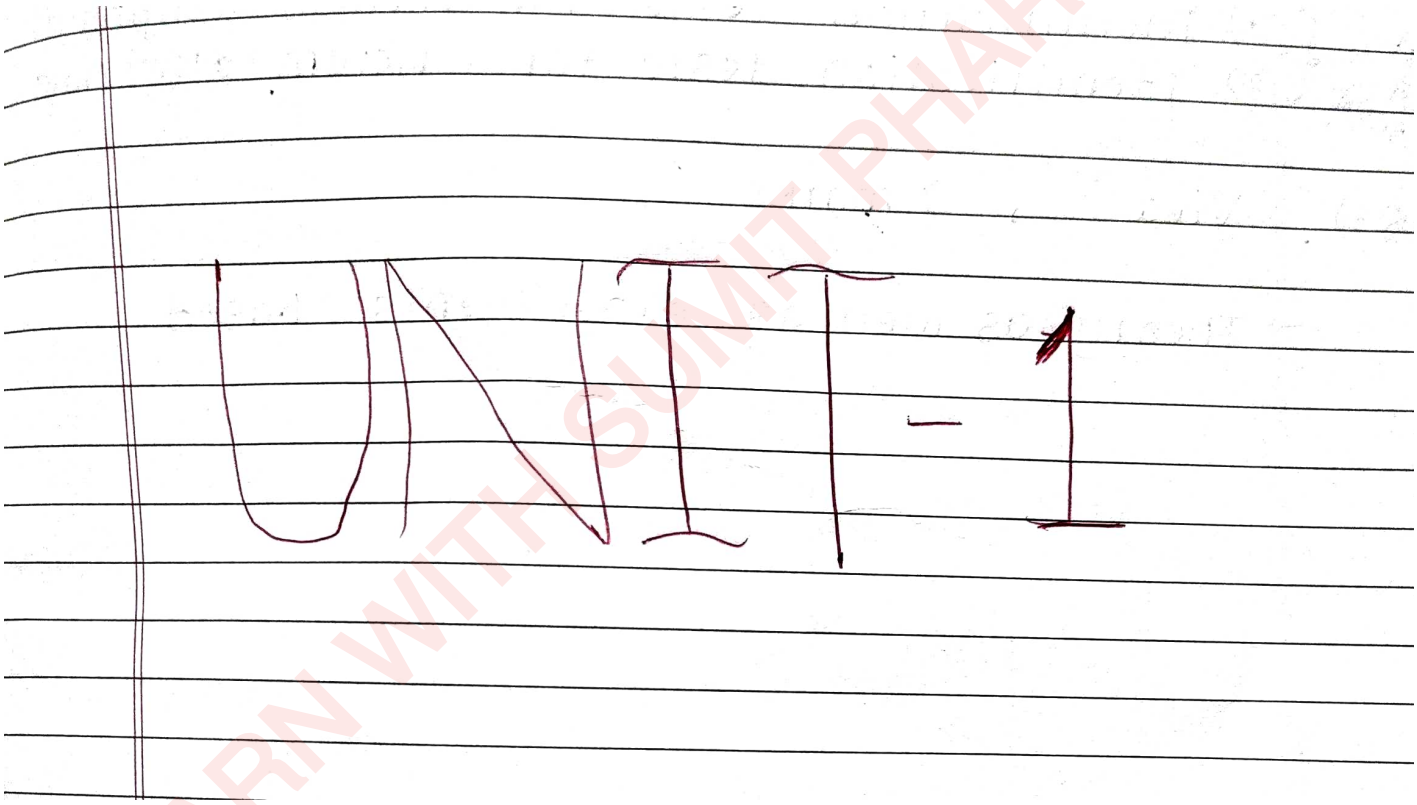

Unit - I

Solubility Of Drugs

- **Solubility →**

The concentration of a substance (solute) can dissolves in a given volume of solvent at a certain temperature to form a homogenous solution.

OR

The spontaneous interaction of two or more substances to form a homogenous molecular dispersion.

- **Solute →** A component which dissolved in the solvent, present in less amount in the Soln.

IMP

- **Solvent →** A component in which solute is dissolved, present in more amount than solute.

- **Solution →** A system in which solutes are completely dissolved in solvent and form a homogenous molecular dispersion.

- **Saturated Solution →** Solution in which the solute in solution is in equilibrium with solid phase.

Imp

Heterogeneous Soln has different phases.

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- **Unsaturated Solution →**

Solution containing dissolved solute in concentration below that necessary for complete saturation.

- **Supersaturated Solution →**

90

Solution containing more of the dissolved solute than it would normally contain.

Imp 2 mark V.V.V. IMP

* **Solubility Expressions →**

Sr. No	Description forms (solubility)	Parts of Solvent required for one part of Solute.
1.	Very Soluble (VS)	< 1
2.	Poorly Soluble (PS)	1 - 10
3.	Soluble	10 - 30
4.	Sparingly Soluble (SPS)	30 - 100
5.	Slightly Soluble (SS)	100 - 1000
6.	Very Slightly Sol. (VSS)	1000 - 10000
7.	Practically insol. (PI)	> 10000

Theory * **Mechanism of Solute Solvent Interaction** →

"Like Dissolves Like"

Sr. No.	Nature of Solvent	Mechanism of Solubility	Example
①	Polar	ⓐ High dielectric constant ⓑ H-bond formation ⓒ dipole interaction	Water + ethanol.
②	Non polar	Weak van der waal's forces.	Fats, oils, alkaloidal bases + CCl_4, benzene.
③	Semi-polar	induce certain degree of polarity	Acetone increase Solubility of ether in water

IMP

Theory * V.IMP **Ideal Solubility Parameters** →

'Ability of a liquid to act as a Solvent'

① Hildebrand Solubility parameter (δ)

IMP "Square root of cohesive energy density"

$$\delta = \sqrt{\Delta H_v - RT / V_m}$$

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② Hansen Solubility parameter (δt)

$\delta t = \delta d + \delta p + \delta h$

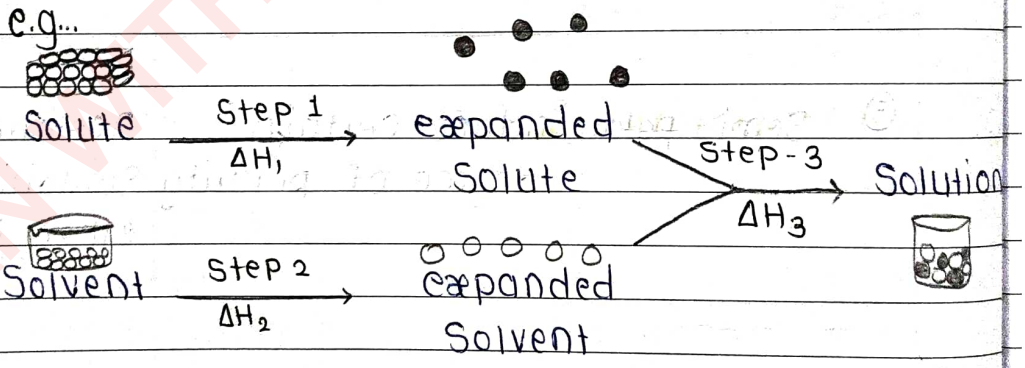
objective* Solvation / Dissolution →

"Interaction of a solute with the solvent, which leads to stabilization of Solute Species in the Solution".

V.IMP
+ve Solvation = endothermic dissolution energy

-ve Solvation = exothermic dissolution energy

e.g...



* Association →

IMP
"Chemical reaction in which the opposite electric charge ions come together in solution and form a distinct chemical entity".

classification according to nature of Interaction :-

① Contact
② Solvent Shared
③ Solvent Separated

IMP *

Factors Influencing Solubility →

① Temperature
② Nature of Solvent (like dissolves like)
③ Pressure
④ pH
⑤ particle size
⑥ Crystal Structure
⑦ Molecular Structure
⑧ Solute - Solvent interaction
⑨ Addition of Substituent
⑩ Common ion effects.
⑪ Solubilizing agents.

① Temperature →

(i) Basically, Solubility increases with temperature. it is the case for most of the Solvents.

(ii) The Situation is though different for gases. with increase of the temparature they became less Soluble in each other and in water, but more Soluble in organic Solvents.

(iii) For example, more Carbon dioxide will dissolve in cold water than in hot water

② Nature of Solvent →

(i) A Solute dissolves in a Solvent when it forms favorable interactions with the Solvent.

(ii) The free energy of Solvation is a combinⁿ of Several factors.

(iii) The creation of the cavity will be entropically and enthalpically unfavorable as the ordered structure of the Solvent decreases

③ Pressure →

(i) Solid and liquid Solutes →

- for majority of Solid and liquid Solutes, pressure does not affect Solubility.

(ii) Gas Solutes →

- As for gasses the Henry's law states that Solubility of gas is directly proportional to the pressure of this gas.

$\therefore P = kC$

Where k is a temperature dependent Constant for a gas.

④ pH →

(i) The pH of an aqueous solution can affect the solubility of the solute, by changing the pH of the solution.

(ii) If the pH of the solution is such that a particular molecule carries no net electric charge, the solute often has minimal solubility.

(iii) The pH at which the net charge is neutral is called the isoelectric point. or pI

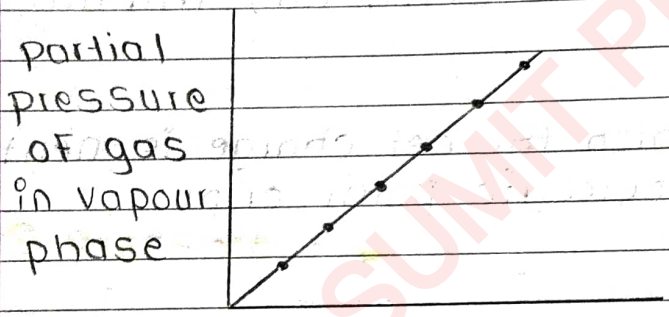
✶ Solubility of Gases in liquids →

IMP

- **Henry's law →**

'Solubility is directly proportional to partial pressure of gas at a constant temp^{e}'

$\therefore S = kP$



✶ Solubility of liquids in liquids →

① Completely miscible liquids :-

e.g...

Water + ethanol,
Glycerine + Alcohol,
benzene + CCl_4

② Partially miscible liquids :-

e.g...

phenol + water

③ Completely immiscible liquids →
e.g...
Mercury + water.

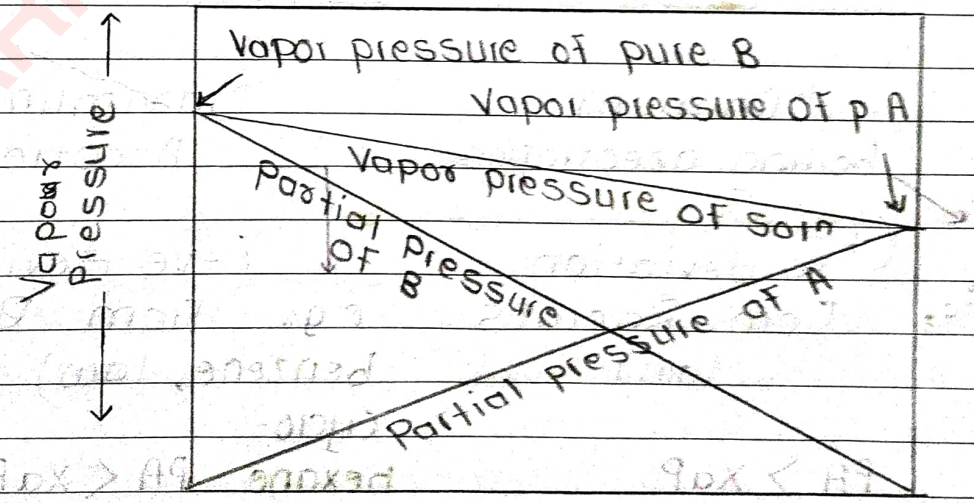
- Raoult's law →

"The partial pressure (p_i) of each component in a solution is equal to the mole fraction of the component and the vapour pressure of the pure component"

$$P_i = xP$$
$$\therefore P = P_A x_A + p_B x_B$$

Imp* Ideal Solutions →

"Solutions which obey Raoult's law in all the solute composition in a solvent".



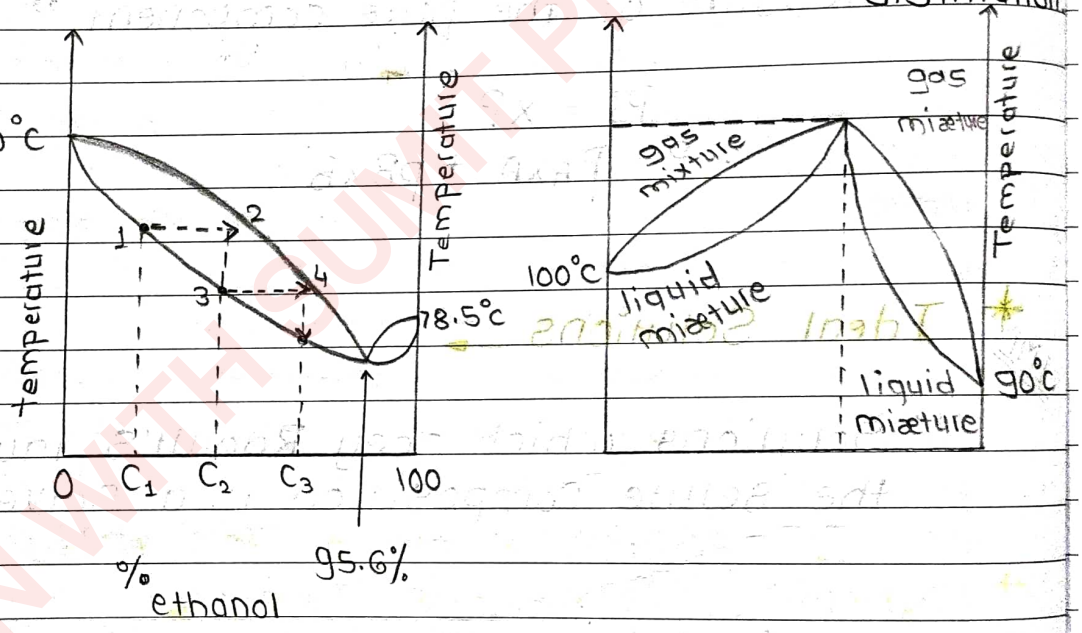
Imp * Real / Non Ideal Solutions →

"Solutions which do not obey Raoult's law over entire range of composition."

* Azeotropes →
(constant boiling mixtures)

def^n → A mixture of 2 liq. which has diffe. B.P & composition throughout distillation

e.g... ethanol, water, Acetone



V. Imp

Minimum boiling azeotropes

e.g... nitric acid, water

(+ve deviation from Raoult's law)

PA > XaP
ΔH > 0
ΔV > 0

Maximum boiling Azeotropes

(-ve deviation from Raoult's law)

e.g... benzene, cyclo-hexane

PA < XaP
ΔH < 0
ΔV < 0

Sparingly Solution are in → 100 - 800

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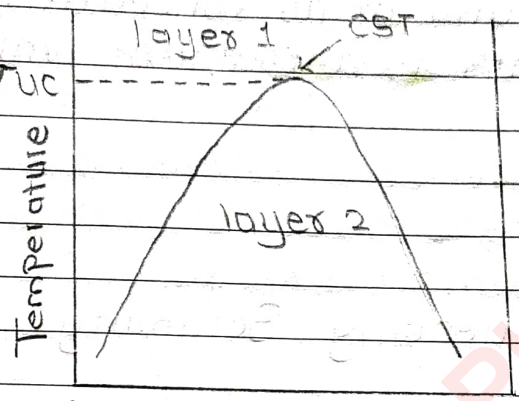
* Critical Solution Temperature → (CST)

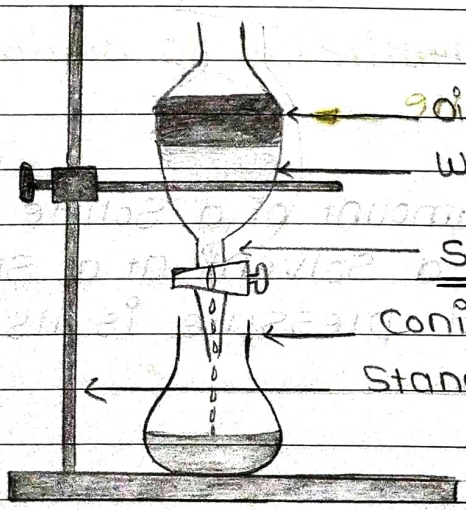
Ex: Phenol & water System



Imp The temperature at which complete miscibility is reached as the temperature is raised or in some cases lowered - used of two liquids that are partially miscible under ordinary conditions, called as CST.

* Nerns't Distribution law → (Partition Coefficient)

Procedure Imp



IMP

"If a Solute distributes between two immiscible Solvents at a constant temp^{e} then the ratio of its Concentration in two Solvents is a constant Value.

$$K = \frac{C_1}{C_2}$$

* Factors Influencing Solubility →

⑤ Particle Size →

(i) Usually, if the particle Size are Smaller, more of the Solute will dissolve faster.

(ii) When minimum particles size accumulat^{n} it takes places.
Hence, particle Size always micro-range

(iii) Particle Size of Solid also effect the Solubility in given Solvent.
These is imp. Concept, reduction achieve micronization.

⑥ Crystal Structure →

(i) The minimum amount of a Solute that can dissolve in a Solvent at a Specified temperature and pressure is its Solubility.

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(ii) The fact that the solubilities decrease as the lattice energy increases.

(7) Molecular Structure →

(i) When a substance dissolves, its molecules or ions separate from one another and become evenly mixed with molecules of the solvent.

(ii) Recall that water contains polar covalent bonds. As a result, water molecules have a negative and positive region.

(8) Solute - Solvent interaction →

(i) The number of -OH groups within a molecule increases solubility in water.

(ii) The more polar bonds in the molecule, the better it dissolves in a polar solvent.
Generalization : "like dissolves like"

(9) Addition of Substituents →

(10) Common ion effect →

(i) The common effect is an example of a Le chatelier's principle

(ii) The presence of a second salt (normally very soluble in water) that produces an ion common to a solubility equilibrium will reduce solubility.

$$AgCl_{(s)} \rightleftharpoons Ag^{+}_{(aq)} + Cl^{-}_{(aq)}$$

(11) Solubilizing Agents →

(i) The Solubility of poorly soluble drug can also be improved by various ~~Stabilizing~~ Solubilizing materials.

(ii) It is preparation of thermodynamically Stable isotropic Solution of a Substance normally insoluble or Slightly Soluble in a given solvent.